

REMARKS

Applicant has amended the specification to remove references to deposits to the American Type Culture Collection (ATCC). Claims 3, 12-20 and 22-25 have been canceled without prejudice and claims 4-8 and 21 have been amended. Support for the amendments made herein lie in the specification and original claims as filed. No new matter has been added by virtue of the amendments.

Applicant gratefully acknowledges that claims 1-2 are allowable.

Objections to the Specification

The Examiner objected to the specification because the ATCC deposit information was left blank.

The specification has been amended to address the objection. It is believed that the amendments contained herein render the present objection moot. Reconsideration and withdrawal of the objection is respectfully requested.

The Rejection of Claims 3 and 6 under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claim 6 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner states that the term "stringent conditions" is indefinite.

In the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, Applicant has amended claim 6 in order to specify the hybridization salt and temperature conditions based on support within the specification, thus rendering the rejection moot. Reconsideration and withdrawal of the rejection is requested.

Claim 3 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner states that the ATCC deposit number is missing.

Applicant has canceled claim 3, thus rendering the rejection moot. Reconsideration and withdrawal of the rejection is requested.

The Rejection of Claims 4-11 and 21 under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 4-11 and 21 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA molecules encoding SEQ ID NO:2 and fragments thereof with eukaryotic kinase activity, does not reasonably provide enablement for any of the following:

- (A) DNA molecules encoding naturally occurring allelic variants of SEQ ID NO:2,
- (B) DNA molecules having 60% identity to SEQ ID NO:1 and 3,
- (C) DNA molecules comprising at least 30 nucleotides of SEQ ID NO:1 or 3,
- (D) DNA molecules encoding a polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO:2,
- (E) DNA molecules which hybridize to SEQ ID NO:1, 3 or any of the above mentioned DNA molecules under "stringent conditions".

Specifically, the Examiner states that the specification teaches that the term "naturally occurring allelic variants" can result in 1-5% variance, but does not teach which residues should be retained for functionality of the protein. The Examiner further states that the "lack of guidance about the structure of critical residues which result in expression products with kinase activity" does not enable DNA molecules that are 30 nucleotides in length, 10 contiguous amino acids, a protein 60% identical to SEQ ID NO:2, or a nucleic acid molecule hybridizing to SEQ ID NO:1 or 3 under "stringent conditions" to encode a functional protein.

Applicant respectfully traverses this rejection, however, in the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, the Applicant has amended claims 4, 5 and 6 to address the issues raised by the Examiner. Specifically, claim 4 has been amended to specify a nucleic acid that is at least 95% homologous to SEQ ID NO:1 or 3, which encodes a naturally occurring variant of a polypeptide comprising SEQ ID NO:2, which has kinase activity. Claim 5 has been amended to specify that the nucleic acid a) comprise a nucleotide sequence which is at least 95% identical to SEQ ID NO:1 or 3; b) comprise a fragment of at least 750 contiguous nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or 3; c) comprise a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence at least 95% identical to SEQ ID NO:2; or d) comprise a fragment of at least 250 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecules of a-d) must encode a polypeptide having kinase activity.

Presently amended claims 4 and 5 recite nucleic acids which are at least 95% identical to the nucleotide sequence of SEQ ID NO:1 or 3, which encode a polypeptide having kinase activity. Claim 5 also recites fragments of at least 750 contiguous nucleotides of SEQ ID NO:1 or 3 encoding a polypeptide with kinase activity or 250 contiguous amino acids of SEQ ID NO:2 having kinase activity. The limitations within these new claims are fully enabled within the specification as Applicant has provided teachings for every element needed for one of skill in the art to practice the claimed invention. Firstly, Applicant has taught that fragments of the polypeptide used in the claimed invention may include sequences of 250 or greater contiguous amino acids (refer to page 2, beginning at line 21). Secondly, Applicant has taught a domain within the eukaryotic protein kinase polypeptide which is conserved and

essential for activity of the polypeptide, namely the eukaryotic protein kinase domain (refer to page 5, line 27 through page 6, line 5). Thirdly, Applicant has provided an example of a specific fragment having at least 250 contiguous amino acids of SEQ ID NO:2 which exhibits the eukaryotic protein kinase activity, namely the eukaryotic protein kinase domain located at about residues 34-285 of SEQ ID NO:2 (refer to page 6, lines 2-5 and figure 3A). Fourthly, by having identified the regions necessary for activity, Applicant has taught which coding regions of the nucleotide sequence which are amenable to alterations as well as those which are not amenable to alterations. The specification teaches one how to generate functional variants of 95% identity by performing nucleotide substitutions leading to amino acid substitutions used in the claimed invention. As defined on pages 16-17, “[c]onservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A ‘conservative amino acid substitution’ is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain.” The Applicant has also defined which of the amino acids have similar side chains, thereby providing a skilled artisan the necessary tools to generate functional variants of the polypeptide used in the claimed invention.

Finally, Applicant has provided teachings for one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired kinase activity. As taught on page 8 of the specification, lines 23-39, such kinase activity can include “interaction with an EPK-55053 substrate or target molecule (e.g., a non-EPK-55053 protein); conversion of an EPK-55053 substrate or target molecule to a product (e.g., transfer of a phosphate group to a substrate or target molecule, or conversion of ATP to ADP); interaction with and/or phosphate transfer to a second non-EPK-55053 protein; modulation of intra- or intercellular signaling and/or gene transcription (e.g., either directly or indirectly); and modulation of the phosphorylation state of EPK-55053 target molecules (e.g., a kinase or a phosphatase molecule) or the phosphorylation state of one or more proteins involved in cellular growth, metabolism, or differentiation, e.g., cardiac, epithelial, or neuronal cell growth or differentiation”. Based on these activities, one can perform assays on specific sequences to determine whether or not such sequences have the desired biological activities. Such assays include, for example, assays which induce a cellular second messenger of the target (e.g., ADP, intracellular Ca^{2+} , diacylglycerol, IP_3 , etc; refer to page 45, lines 31-37). Performing such assays to determine whether or not an allelic variant of 95% identity to SEQ ID NO:1 or 3 or a fragment of SEQ ID NO:2 has the desired properties would not constitute undue experimentation. Therefore, Applicant has provided all of the necessary information to enable one of skill in the art to 1) identify regions within the polypeptide of the claimed invention which may be altered while maintaining activity; 2) generate fragments; and 3) perform assays to determine whether or not the sequences generated do in fact have the desired kinase activity.

Therefore, contrary to the Examiner's assertions, Applicant has provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably

correlated with the scope of amended claims 4-5. As previously stated above, claim 6 has been amended to specify the hybridization salt and temperature conditions. It is believed these claim amendments render the present 35 U.S.C. § 112, First Paragraph rejection over claims 4 and 5, as well as claims which depend upon claims 4 and 5, namely claims 6-11 and 21 moot. Applicant respectfully requests reconsideration and withdrawal of the 35 U.S.C. § 112, First Paragraph rejection over claims 4-11 and 21.

The Rejection of Claims 4-11 and 21 under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 4-11 and 21 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that claims 4-6 and their dependent claims 7-11 and 21 are directed to the genera of DNA molecules in (A)-(E) above which have not been adequately described in the specification. The Examiner asserts that these genera of DNA molecules could potentially encode many different functionally unrelated proteins and that the specification discloses only one species.

In the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, Applicant has amended claims 4-6 as described above.

As recited above, amended claims 4-5 recite nucleic acid molecules which are 95% identical to SEQ ID NO:1 or 3, wherein the nucleic acid molecule encodes a polypeptide having kinase activity. The claims also recite nucleic acid fragments encoding a polypeptide comprising at least 250 contiguous amino acids of SEQ ID NO:2, wherein the polypeptide has kinase activity. In light of these newly presented claims, Applicant traverses the Examiner's rejection and argue that they were in possession of the claimed invention at the time of filing for the reasons discussed below.

The Examiner is of the opinion that Applicant had not disclosed the claimed genus of DNA molecules of SEQ ID NO:1 or 3 in the specification and hence were not entitled to such genus claims. The Examiner also states that “[m]any functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species (DNA sequences encoding SEQ ID NO:2) of the claimed genera which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genera.” Contrary to the Examiner's assertion, the specification not only provides the sequence of the nucleic acid molecule of the claimed invention (SEQ ID NO:1 and 3), but also provides for nucleic acid molecules which are at least 95% identical to SEQ ID NO:1 or 3 and fragments that falls within the scope of the new claims, namely the nucleic acids that encode at least the eukaryotic protein kinase domain, as well as extensive teachings as discussed above, to obtain other functionally active fragments which fall within the scope of the new claims. Therefore, by having provided the full length sequence of the nucleic acid molecule of the claimed invention, a nucleic acid that encodes a functional fragment of the polypeptide of the claimed

invention having the desired activity, and an enabling disclosure for obtaining other such functional sequences, Applicant has provided the necessary teachings to demonstrate that they were in possession of the claimed invention at the time of filing.

In view of the amendments and remarks discussed above, reconsideration and withdrawal of the 35 U.S.C. 112, first paragraph rejection over claims 4-11 and 21 is respectfully requested.

The Rejection of Claims 5 and 6 under 35 U.S.C. § 102 Should Be Withdrawn

Claims 5-6 were rejected under 35 U.S.C. 102(b) as being anticipated by Cheret et al. The Examiner states that Cheret teaches a DNA sequence that encodes a polypeptide comprising a fragment of SEQ ID NO:2 of at least 10 contiguous amino acids prior to this invention, anticipating claim 5, and is capable of hybridizing to the DNA molecule of 5(d), anticipating claim 6.

In the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, Applicant has amended claim 5(d) to specify a fragment of at least 250 contiguous amino acids, rendering the present 35 U.S.C. 102(b) rejection over claims 5 and 6 moot. Reconsideration and withdrawal of the rejection is respectfully requested.

The Rejection of Claims 7-11 and 21 under 35 U.S.C. § 103 Should Be Withdrawn

Claims 7-11 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cheret in view of either current gene expression techniques or gene detection techniques. The Examiner asserts that even though Cheret does not teach fusion products, vectors and host cells comprising the DNA sequence that encodes a polypeptide (YKL453), comprising a fragment of SEQ ID NO:2 of at least 10 contiguous amino acids, it would have been obvious to one of ordinary skill of the art to start with the DNA sequence of Cheret and place it in an appropriate vector and host for gene detection or expression or in a kit.

In the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, Applicant has amended claim 5(d) to specify a fragment of at least 250 contiguous amino acids, rendering the present 35 U.S.C. 103(a) rejection over claims 7-11 and 21 moot. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSIONS

In view of the amendments and remarks made herein, Applicant respectfully submits that the objections and rejections presented by the Examiner are now overcome and that this application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

This paper is being filed timely, and no extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

September 02, 2003

MILLENNIUM PHARMACEUTICALS, INC.

By



Tracy M. Sioussat
Registration No. 50,609
75 Sidney Street
Cambridge, MA 02139
Telephone - 617-374-7679
Facsimile - 617-551-8820